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ORCIPRENALINE CHRONIC EFFECT IN BYSSINOSIS

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Exposure to textile dust has been reported to produce byssinosis with bronchospasms as a major pathogenic mechanism.

In the present study 228 exposed workers in a hemp flax mill were examined. The subjects were followed up during several successive years.

The therapy was conducted intermittently for one year, by alternating orciprenaline with phenoterol and using 0.75—1.50 mg of Alupent, and 0.2—0.4 mg of Berotec, Boehringer Ingelheim, respectively. These drugs were administered before the shift, on Monday, Tuesday, Wednesday and Friday, which are regarded as the »critical days« of byssinosis. In 67—84 percent of the cases an attenuation was registered, the medication showing to suppress the Monday syndrome consisting of chest tightness, dyspnoea and cough. On Monday, the FEV_1 values tended to become normal in 34 per cent of the cases and to improve in 29 per cent of the cases. The improvement was of long duration, the FEV_1 values remaining within normal limits for several months, and paradoxically, even a decrease was noted in 63—94 per cent of the persons with clinical symptoms but without functional disorders.

Our data allow the following conclusions: 1. There are two clinical forms of byssinosis — a) Manifest byssinosis, and b) Incomplete byssinosis with clinical symptoms but without functional modifications. 2. Pathogenic treatment with adrenergic bronchospasmolytics is effective, suppressing the Monday syndrome in 63 per cent of cases. It is recommended in cases of manifest byssinosis, while in incomplete byssinosis the indication is relative and requires biannual spirographic measurements. In the case of exposed but asymptomatic workers the treatment is inadvisable.

Byssinosis has been considered to be an occupational disease generated by dust in the textile industry during the soft hemp, flax and cotton dry mechanical manufacture.

In spite of numerous research the actual etiological agent of byssinosis which is present in a dust complex of vegetable, microbial and

mineral origin, has not yet been identified. Although the clinical and functional aspects are fairly well defined (1) there are still unsolved problems concerning the diagnosis of byssinosis. This fact is confirmed by the marked differences regarding its prevalence. Some authors (2—7) have reported a prevalence of between 4—15 per cent, whereas others (8—12) have found percentages varying from 25 to 80. In our previous studies, in a group of more than 1500 exposed workers the prevalence of workers complaining of symptoms typical of byssinosis was found to surpass about 2—3 times those presenting functional modifications at the same time.

Until now, the only known pathogenic mechanism has been the bronchospasm. Based on this and on similar data, we observed orciprenaline effects solely in byssinotic subjects presenting pathological spirographic values; in persons having clinical symptoms without spirographic modifications, orciprenaline either induced a broncho-constrictive effect or was even ineffective.

Recently, byssinosis has been described as »scheduled asthma« (13), being differentiated from asthma of various etiology by the facts that it is specifically correlated with the time of exposure (the Monday syndrome) and that chest tightness exceeds wheezing.

Numerous studies published recently deal with respiratory modifications (14, 15, 16) especially with the administration of various drugs in byssinosis: *Bouhuys* reported on studies with a phenothyazinic substance (17), *Valić* with orciprenaline, diadril and ascorbic acid (18) and *Kamat* with orciprenaline, isoprenaline, salbutamol, ephedrine (19, 20, 21) etc.

Nervous receptors in the alveolar and bronchial walls have lately been described, with preponderance in their respective muscularity, besides the well known adrenergic and cholinergic receptors reported by *Ahlquist*. Some of them may induce sensations such as »air thirst« and respiratory discomfort (22). At the same time, *Kamat* (3) distinguishes between byssinosis with complete symptomatology and byssinosis presenting only a work-related cough.

In the light of the above we became convinced of the need for an adequate and systematic treatment and medical surveillance of the existing various clinical forms of byssinosis.

SUBJECTS AND METHODS

The research was conducted on 228 workers exposed to soft hemp and flax dust in a hemp-flax mill. There were 149 workers with byssinosis (38 with manifest symptoms, and 111 with clinical symptoms only, but having normal lung function tests), 66 cases with respiratory subjective disorders, and 13 cases having other intercurrent or chronic

respiratory disorders. This longitudinal study was aimed at establishing a diagnosis by means of repeated tests based on clinical and functional chronic modifications. The investigations were carried out with a questionnaire according to *Schilling's* principles, while the spirographic measurements with a »Vitalograph« were carried out during the workshift, near the workplace, four times a week: on Monday, Tuesday, Wednesday and Friday. The spirographic values were related to the CECA (Communauté Européenne du Charbon et d'Acier) normal values. In our study, according to literature, we used the FEV_1 parameter (forced expiratory volume in one second). The therapy was focused on controlling the bronchospasm by alternating orciprenaline with phenoterol: Alupent and Berotec Boehringer, Ingelheim, respectively. One or two puffs from the original sprayer were administered: 0.75—1.50 mg of Alupent, and 0.2—0.4 mg of Berotec. Medication was given before the shift during the first three days of the week, i. e. the »critical days« of the disease.

The results of the therapy were verified after one year of treatment, in comparison with the symptoms before the therapy.

RESULTS

The present study suggests a difference between the clinical and functional effectiveness of the therapy. While most subjects claimed to feel a marked improvement from the clinical point of view, their functional response depended on the initial functional stage.

An attenuation of clinical symptoms (chest tightness, dyspnoea, cough), was reported in 67—84 per cent of the cases, with both normal and pathological lung function tests.

Table 1.

Therapeutic effect (in per cent) of orciprenaline and phenoterol on clinical symptoms in byssinosis (n = 149)

Diagnosis	Chest tightness		Dyspnoea		Cough	
	Attenuated	Unmodified	Attenuated	Unmodified	Attenuated	Unmodified
Manifest byssinosis (n = 38)	84.2	15.8	73.7	26.3	71.1	28.9
Incomplete byssinosis (n = 111)	70.0	30.0	77.0	23.0	67.0	33.0

It is of interest that cough showed to be influenced by the treatment to a lesser extent, persisting in 28.9—33 per cent of the subjects after treatment. Several possible factors may explain this finding, the most important being an irritative and loading action of the upper respiratory tract. *Kamat* (3) reported an aspect of byssinosis manifested by only a work-related cough. The therapy with orciprenaline and phenoterol administered in our studies was »bronchospasmolytic« rather than »bronchodilating«. The high effectiveness of these drugs became manifest in 63 per cent of cases of bronchospasm suppressing the »Monday syndrome«, and even normalizing lung functions in 34 per cent of the cases.

Table 2

Therapeutic effect of orciprenaline and phenoterol on lung functions (FEV_1) in manifest byssinosis (n = 38)

FEV_1	Monday		Tuesday		Wednesday		Friday	
	% of normal values	% cases	% of normal values	% cases	% of normal values	% cases	% of normal values	% cases
Increase	72—92	63	77—94	48	76—88	35	64—69	**17**
— restitution		34		21		14		—
— attenuation		29		27		21		17
Decrease	84—68	37	85—71	52	99—84	65	100—86	83

Table 3

Therapeutic effect of orciprenaline and phenoterol on lung functions (FEV_1) in incomplete byssinosis (n = 111)

FEV_1	Monday		Tuesday		Wednesday		Friday	
	% of normal values	% cases	% of normal values	% cases	% of normal values	% cases	% of normal values	% cases
Increase	95—107	9	100—110	3	113—116	9	116—120	17
Decrease	123—110	82	120—109	94	121—107	79	122—112	80
Unmodified		9		3		12		3

In cases without bronchospasms, i.e. with normal FEV_1 values, a paradoxical effect was noticed, even in chronic intermittent administration for one year. In 63—94 per cent of the cases a decrease of FEV_1 values was registered, both in subjects with clinical symptoms and in asymptomatic cases.

Table 4

Therapeutic effect of orciprenalin and phenoterol on lung functions (FEV_1) in asymptomatic, exposed workers (n = 66)

FEV_1	Monday		Tuesday		Wednesday		Friday	
	% of normal values	% cases	% of normal values	% cases	% of normal values	% cases	% of normal values	% cases
Increase	114—125	34	118—126	18	107—121	12	129—132	15
Decrease	123—112	63	124—114	82	127—115	85	127—115	85
Unmodified		3		—		3		—

The described modifications were also observed during a previous study concerning acute FEV_1 failure after Alupent administration (23). However, our assertion has been confirmed in cases of other chronic or intercurrent respiratory diseases (see Table 5).

Table 5.

Therapeutic effect of orciprenaline and phenoterol on lung functions (FEV_1) in exposed workers with other chronical or intercurrent diseases (n = 13)

FEV_1	Monday		Tuesday		Wednesday		Friday	
	% of normal values	% cases	% of normal values	% cases	% of normal values	% cases	% of normal values	% cases
Increase	73—83	30	70—79	25	78—93	60	69—85	50
Decrease	91—76	70	90—75	75	88—71	40	95—77	50
Unmodified		—		—		—		—

The FEV_1 increase under this therapy was evident from comparison with FEV_1 values obtained before treatment; in cases with initially normal FEV_1 range, this parameter decreased. The decrease was due to other factors (oedema, hypersecretion) because in the absence of spasms the treatment proved ineffective.

DISCUSSION AND CONCLUSION

The present paper supports the view that there are two clinical forms of byssinosis: manifest byssinosis associated with chest tightness, dyspnoea and cough with accompanying disorders of the pulmonary functions and incomplete byssinosis showing clinical symptoms on the first day or in the first half of the week, but with unmodified values of the functional parameters (FEV_1 exceeding 80 per cent of the normal values). The former shows described clinical symptoms and a FEV_1 value under 80 per cent of the normal values; it is also of interest that the first day's work, after a break of at least 24 hours, appears to be the worst of the whole week.

In patients with incomplete byssinosis functional values as presented in Table 3 remain strictly within the normal range.

As is well known, respiratory discomfort may well be associated with chest tightness, dyspnoea and cough without an impairment of the pulmonary functions; the nervous sensitive receptors involved in this phenomenon have been described in detail by *Paintal* and co-workers (22).

It should also be noted that only a small percentage of the cases degenerated into manifest byssinosis, while other subjects presented the same unmodified phenomenon for a period of 20 years or more; it may be regarded as a clinical form connected with individual reaction to the pathogenic agent.

Treatment with bronchospasmolytic sympathomimetics is based upon the well known pathogenic mechanism of byssinosis and their own great effectiveness. Therefore we consider it as a specific treatment rather than a symptomatic one, particularly because it suppresses the Monday syndrome, i.e. the clinical as well as functional manifestation of the disease. The beneficial effect lasts throughout the week in cases of increased or decreased FEV_1, the latter presenting a trend towards normal values.

In view of the effectiveness of pre-shift inhalatory treatment for the prevention of bronchospasms in the Monday syndrome, attention has been focused on the pathogenicity of byssinosis by the application of a curative prophylactic therapy. It should be emphasized that the major problem of sclerosis and prevention of cor pulmonale is still unsolved and requires further investigation.

In connection with the above we would recommend this treatment, especially with orciprenaline, in the following manner:

a) In cases of manifest byssinosis, 1—2 pre-shift puffs during the first three days of the week. Exceptionally, in some workers a repeated treatment on the same day is indicated, but on the whole in most workers the therapy should be reduced to a single week dose.

b) In incomplete byssinosis, the therapy has only a relative indication, and the spirographic parameters should be checked every 6 months.

c) In the case of exposed but asymptomatic workers this treatment is not recommended.

In addition to these active measures, attention should also be paid to the health risks due to textile dusts, by eliminating the etiological agent and providing absolute protection. Also, longer lasting follow-up studies should be undertaken in order to clarify the problem of chemical substances used in technological processes.

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Sažetak

DUGOTRAJNI UČINCI ORCIPRENALINA U BISINOZI

Poznato je da ekspozicija tekstilnoj prašini izaziva bisinozu, bolest u kojoj je glavni patogenetski mehanizam povezan s bronhospazmom. U ovom su radu opisani rezultati ispitivanja 228 radnika zaposlenih u predionici konoplje i lana, koji su praćeni nekoliko uzastopnih godina.

Terapija što su je primijenjivali u određenim vremenskim razmacima sastojala se od naizmjenične primjene orciprenalina s fenoterolom odnosno primjene 0,75/1,50 mg Alupenta i 0,2—0,4 mg Beroteca. Ove su lijekove radnici uzimali prije početka rada, ponedjeljkom, utorkom, srijedom i petkom, dakle u dane koji se smatraju kritičnim za bisinozu. U 67—84% pacijenata utvrđeno je olakšanje simptoma posebice s obzirom na stezanje u prsima, dispneju i kašalj. U 34% ispitivanih radnika vrijednosti za FEV_1 su se normalizirale a u 29% vrijednosti su se poboljšale. Poboljšanje je bilo dugotrajno, čak po nekoliko mjeseci.

Na temelju postignutih rezultata moglo bi se zaključiti da postoje dvije forme bisinoze: manifestna i inkompletna, tj. s kliničkim simptomima, ali bez funkcionalnih promjena. Također se moglo zaključiti da je primjena adrenergičnih bronhospazmolitika vrlo djelotvorna jer se takvom terapijom moglo stanje olakšati čak u 63% pacijenata. Stoga se terapija preporuča samo za manifestne oblike bisinoze, ali ne i za radnike koji nemaju simptoma.

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